UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,453	07/18/2006	Matthew David Osborne	BJS-620-412	4519

23117 7590 10/07/2010

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
MARVICH, MARIA	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
10/07/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,453	OSBORNE ET AL.	
	Examiner	Art Unit	
	MARIA B. MARVICH	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-10,13-16,33,36-41 and 43-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-10,13-16,33,36-41 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/6/10 has been entered.

Claims 1, 4-10, 13-16, 33, 36-41 and 43-50 are pending in this application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5-10, 14-16, 33, 36, 37-41, 43 and 46-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Field et al (US 6,593,140; see entire document). **This rejection is maintained as upon reconsideration of the phrase "about 0.064 mg/L", it does not explicitly rule out the teachings of Field et al which teach use of 0.03 mg/L. About is relative and the range being as large as it is does not exclude one from considering 0.03 to be about 0.064.**

Myeloma cells were cultured *in vitro* in media lacking transferrin and tropolone (lipophilic chelator) but in the presence of 0.2 mg/l of ferric ammonium citrate in suspension culture (see e.g. example 5, line 29-31). As depicted in figure 1, the control cultures do not contain chelators. The disclosure of Fields et al states that the cells do not survive after 48 hours.

Nonetheless, the cells are cultured in media meeting the requirements of the instant claims. Furthermore, as the media requirements overlap that of the instant claims, one would expect those of Fields et al to be as successful as that of the instant claims. As evidenced by the instant specification, the concentration of 1.25 mg/L of ferric ammonium citrate is about 0.2 mg/L of iron. Hence, the iron concentration is about 0.03 mg/L. The media was serum-free see example 2.

Claims 1, 4-7, 33, 36-41 and 45-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Gorfien et al (US 20060148074; see entire document). **Gorfien et al teach that the iron concentration is 0.28-11 mg/L which falls within the recite range of 0.64-1.6 as well as 0.16-0.32.**

Myeloma cells were cultured *in vitro* in suspension culture in media lacking transferrin, lipophilic chelators and nitrogen containing chelators but in the presence of ferric chloride-sodium citrate (see e.g. ¶ 0094). Iron is in the concentration of **0.28 mg/L to 11 mg/L** (see e.g. ¶ 0113). As evidenced by the instant specification, the concentration of 1.25 mg/L of ferric ammonium citrate is about 0.2 mg/L of iron.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-10, 13-16, 33, 36-41 and 43-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Field et al (US 6,593,140; see entire document) in view of Gorfien et al (US 20060148074; see entire document). **This rejection is maintained for reasons above.**

Applicants claim a method of culturing myeloma cells in media lacking transferring, lacking lipophilic chelators and lacking synthetic and/or lipophilic nitrogen containing chelators and in the presence of ferric ammonium citrate.

The teachings of Field and Gorfien et al are described above. Gorfien teaches media for culturing myeloma wherein the iron concentration is between 0.28 and 11 mg/L Hence, the iron concentration would be about 1.75-68.75 mg/L of ferric ammonium citrate.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use ferric ammonium citrate as taught by Field et al in the media taught by Gorfien et al because Gorfien et al teach that it is within the ordinary skill of the art to use particular levels of iron to culture myeloma cells and because Gorfien et al teach that it is within the ordinary skill of the art to use ferric ammonium citrate as a source of iron. In KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007), the Supreme Court particularly emphasized "the need for caution in granting a patent based on a combination of elements found in the prior art," (Id. At 1395) and discussed circumstances in which a patent might be determined to be obvious. Importantly, the Supreme Court reaffirmed principles based on its precedent that obviousness in part is predicated on use of particular known techniques that are recognized as part of the ordinary capabilities of one skilled in the art. In the instant case, Gorfien and Field et al are both directed at methods of culturing myeloma cells. The combination of the two represents the combination of familiar elements according to known methods is likely to be

obvious when it does no more than yield predictable results." (Id. At 1395.) Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to applicants' arguments

Applicants have traversed the rejection under 35 USC 102 in the amendment filed 3/5/10. First, applicants argue that aside from falling outside of the new range for ferric ammonium citrate concentration does not demonstrate growth of the culture, which according to the specification is described by at least a doubling or preferably a tripling. As set forth above, the new range does not exclude the instant teachings. Applicants argue that Gorfien does not exemplify growth of myeloma cells in iron containing medium only Cho and 293 cells. Gorfien et al is directed toward development of media for high density growth of cells and to this end, Gorfien most explicitly intends myeloma cells. While Gorfien et al do not exemplify myeloma does not teach away from use of myeloma cells with the media. Applicants are not limited to what they exemplify but to what the encompass.

> [0153] In a preferred embodiment, the replacement medium of the present invention is used to grow CHO cells in suspension culture. In another preferred embodiment, the replacement medium of the present invention is used to grow hybridoma cells in suspension culture. In yet another preferred embodiment, the replacement medium of the present invention can be used to culture NS/O myeloma cells in suspension culture. If NS/O myeloma cells are cultured, the replacement 1.times. medium of the present invention can be supplemented with a lipid mixture supplement (see Table 3).

The replacement media also most explicitly contains iron in place of transferrin.

[0112] In the replacement media of the invention, any basal media may be used. Such basal media may contain one or more amino acids, one or more vitamins, one or more inorganic salts, one or more buffer salts, and one or more lipids. In accordance with the invention, **transferrin is replaced with iron or an iron-containing compound a**nd/or insulin is replaced with zinc or a zinc containing compound. Preferably, iron chelate compounds are used in accordance with the invention

[0113] Fe.sup.2+ and/or Fe.sup.3+ chelate compounds which may be used include but are not limited to compounds containing an Fe.sup.2+ and/or Fe.sup.3+ salt and a chelator such as ethylenediaminetetraacetic acid (EDTA), ethylene glycol-bis(.beta.-aminoethyl ether)-N,N,N,N'-tetraacetic acid (EGTA), deferoxamine mesylate, dimercaptopropanol, diethylenetriaminepentaacetic acid (DPTA), and trans-1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (CDTA). For example, the iron chelate compound may be a ferric citrate chelate or a ferrous sulfate chelate. Preferably, the iron chelate compound used is ferrous sulphate.7H.sub.2O EDTA (FeSO.sub.40.7H.sub.2O EDTA, e.g., Sigma F0518, Sigma, St. Louis, Mo.). In the medium of the present invention, the concentration of Fe.sup.2' and/or Fe.sup.3+ can be optimized using only routine experimentation. **Typically, the concentration of Fe.sup.2+ and/or Fe.sup.3+ in the 1.times. medium of the present invention can be about 0.00028 to 0.011 g/L.** Preferably, the concentration of iron is about 0.0011 g/L.

Applicants argue that Field et al teach that transferring or tropolone must be present for use of ferric ammonium citrate. To the contrary, Field et al teach

> In the absence of either tropolone or transferrin but in the presence of 0.2 mg/l ferric ammonium citrate myeloma cells failed to thrive and died within 48 hours.

As regards applicants' arguments regarding the growth of the cells, the art teaches that *in vitro* cultured myeloma cells can have a doubling time of about 35 hours, hence within 48 hours, one would expect the cells to have doubled. The instant claims only require inoculation of the medium and growth. The lack of long term growth is not excluded by the claims. However, it is noted that Gorfien improves upon these methods by increasing the concentration of iron and the combination of methods would be expected to lead to improved growth conditions.

As to Gorfien et al, applicants argue that the reference does not teach that the cells were grown in agitated suspension culture. Gorfien et al is directed to a cell culture medium for *in vitro* cultivation of cells in suspension. Specifically cited are NS/O myeloma cells. Specifically, applicants teach that the taught media can be used specifically to culture these cells. While long term cultivation is not possible with the conditions, the basic limitations of the claim are met.

Applicants argue that Gorfien et al do not teach growth with agitation. Gorfien et al teach that "For suspension cultivation, cells are typically suspended in the present culture media and introduced into a culture vessel that facilitates cultivation of the cells in suspension, such as a spinner flask, perfusion apparatus, or bioreactor (see Freshney, R. I., Culture of Animal Cells: A Manual of Basic Technique, New York: Alan R. Liss, Inc., pp. 123-125 (1983)). Ideally, agitation of the media and the suspended cells will be minimized to avoid denaturation of media

components and shearing of the cells during cultivation." It is noted that myeloma cells are grown in suspension and hence subjected to the media and culturing conditions taught as a whole by Gorfien et al. While Gorfien et al teach that agitation is kept to a minimum, there is no absence of agitation. Hence, as a whole Gorfien et al teach methods of culturing myeloma cells using media meeting the conditions of the instant claims wherein the cells are grown i.e. in spinner flasks. Spinner flasks and other forms of culturing for suspension cells require that some agitation be present.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD
Primary Examiner
Art Unit 1633

/Maria B Marvich/
Primary Examiner, Art Unit 1633